

AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions, and listings, of claims in the application:

1. (previously presented) A solid pharmaceutical composition comprising a mixture of:
 - (a) an active macromolecular principle which is a polypeptide or protein, polynucleotide or polysaccharide;
 - (b) a non-conjugated bile acid or salt; and
 - (c) an additive chosen from
 - (i) propyl gallate or a linear or branched chain C₁₋₁₂ alkyl, C₁₋₁₂ alkyloxy, C₁₋₁₂ alkylthio or C₂₋₁₂ alkenyl ester of gallic acid which is optionally substituted with one or more groups which are the same or different and are selected from halogen and linear or branched chain C₁₋₁₂ alkyl, C₁₋₁₂ alkyloxy, C₁₋₁₂ alkylthio or C₂₋₁₂ alkenyl;
 - (ii) butyl hydroxy anisole, or hydroxy anisole wherein the methoxy group linked to the aromatic ring and/or the hydrogen *ortho* to the hydroxyl group is/are replaced by one or more groups which are the same or different and are selected from linear or branched chain C₁₋₁₂ alkyl, C₁₋₁₂ alkyloxy, C₁₋₁₂ alkylthio and C₂₋₁₂ alkenyl, either unsubstituted or substituted in any position by one or more halogen atoms; and
 - (iii) a mixture of (i) and (ii)

wherein the mixture comprises at least 1% by weight of the additive (c), wherein the ratio by weight of the non-conjugated bile salt + additive (b+c) to the active macromolecular principle is at least 3:1 and wherein the composition, when introduced into the intestine, does not raise the pH of the intestinal fluid above pH 7.0.

2. (original) A composition according to claim 1, which comprises less than 5% by weight of water.

3.-4 (canceled).

5. (previously presented) A composition according to claim 1, wherein the ratio by weight of the non-conjugated bile salt+additive (b + c) to the active macromolecular principle is at least 5:1.

6. (previously presented) A composition according to claim 1, wherein the mixture is in the form of a solution or a microparticulate dispersion.

7. (previously presented) A composition according to claim 1, wherein the mixture is in solid form.

8. (canceled).

9. (currently amended) A composition according to claim 1, where the active macromolecular principle is chosen from insulin, calcitonin, growth hormone, parathyroid hormone, erythropoietin, GLP1 and GCSF, ~~and derivatives and analogues thereof, either synthetic or from natural sources, conforming to structures derived from either human or animal origin,~~ or is single, double or triple-stranded RNA.

10. (currently amended) A composition according to claim 9, where the active macromolecular principle is insulin, calcitonin~~[[,]]~~ or parathyroid hormone ~~or a derivative or analogue thereof, either synthetic or from natural sources, conforming to structures derived from either human or animal origin.~~

11. (currently amended) A composition according to claim 10, wherein the active macromolecular principle is insulin ~~or a derivative or analogue thereof, either synthetic or from~~

~~natural sources, conforming to structures derived from either human or animal origin, and the~~
composition further comprises an insulin sensitizing agent.

12. (previously presented) A composition according to claim 1, wherein component (b) is chenodeoxycholate.

13. (previously presented) A composition according to claim 1, wherein the additive is propyl gallate or a linear or branched chain C₁₋₁₂ alkyl, C₁₋₁₂ alkyloxy, C₁₋₁₂ alkylthio or C₂₋₁₂ alkenyl ester of gallic acid which is optionally substituted with one or more groups which are the same or different and are selected from halogen and linear or branched chain C₁₋₁₂ alkyl, C₁₋₁₂ alkyloxy, C₁₋₁₂ alkylthio or C₂₋₁₂ alkenyl.

14. (previously presented) A composition according to claim 1, wherein the additive is butyl hydroxy anisole or hydroxy anisole where the methoxy group linked to the aromatic ring and/or the hydrogen ortho to the hydroxyl group are replaced by linear or branched chain C₁₋₁₂ alkyl, C₁₋₁₂ alkyloxy, C₁₋₁₂ alkylthio or C₂₋₁₂ alkenyl, either unsubstituted or substituted in any position by one or more halogen atoms.

15.-18. (canceled).

19. (currently amended) A method according to claim 26 wherein the active macromolecular principle to be absorbed is chosen from insulin, calcitonin, growth hormone, parathyroid hormone, erythropoietin, GLP1 and GCSF, ~~and derivatives and analogues thereof, either synthetic or from natural sources, conforming to structures derived from either human or animal origin,~~ or is single, double or triple-stranded RNA.

20. (currently amended) A method according to claim 19, wherein the active macromolecular principle to be absorbed is insulin, calcitonin, or parathyroid hormone ~~or a~~

~~derivative or analogue thereof, either synthetic or from natural sources, conforming to structures derived from either human or animal origin.~~

21. (currently amended) A method according to claim 20, wherein the active macromolecular principle to be absorbed is insulin ~~or a derivative or analogue thereof, either synthetic or from natural sources, conforming to structures derived from either human or animal origin~~, and an insulin sensitizing agent is also present.

22. (previously presented) A method according to claim 26, wherein the composition comprises less than 5% by weight of water.

23. (previously presented) A method according to claim 26, wherein the active macromolecular principle which is a polypeptide or protein, polynucleotide or polysaccharide, the non-conjugated bile acid or salt and the additive are formulated as a solution, a microparticulate dispersion or a solid.

24. (previously presented) A method of enhancing the absorption of a active macromolecular principle in a patient, which method comprises administering to said patient a composition as defined in claim 1.

25. (canceled).

26. (previously presented) A method of enhancing the absorption of an active macromolecular principle which is a polypeptide or protein, polynucleotide or polysaccharide across the intestinal wall in a human or animal body, which method comprises administering a non-conjugated bile acid or salt, together with an additive chosen from:

- (i) propyl gallate or a linear or branched chain C₁₋₁₂ alkyl, C₁₋₁₂ alkyloxy, C₁₋₁₂ alkylthio or C₂₋₁₂ alkenyl ester of gallic acid which is optionally substituted with one or more groups which are the same or different and are selected from halogen

and linear or branched chain C₁₋₁₂ alkyl, C₁₋₁₂ alkyloxy, C₁₋₁₂ alkylthio or C₂₋₁₂ alkenyl;

- (ii) butyl hydroxy anisole, or hydroxy anisole wherein the methoxy group linked to the aromatic ring and/or the hydrogen *ortho* to the hydroxyl group is/are replaced by one or more groups which are the same or different and are selected from linear or branched chain C₁₋₁₂ alkyl, C₁₋₁₂ alkyloxy, C₁₋₁₂ alkylthio and C₂₋₁₂ alkenyl, either unsubstituted or substituted in any position by one or more halogen atoms; and

- (iii) a mixture of (i) and (ii)

together with the active macromolecular principle in a solid pharmaceutical composition, wherein the additive accounts for at least 1% by weight of the total weight of (a) the active macromolecular principle, (b) the non-conjugated bile acid or salt, plus (c) the additive, wherein the ratio by weight of the non-conjugated bile salt + additive (b+c) to the active macromolecular principle is at least 3:1 and wherein the composition, when introduced into the intestine, does not raise the pH of the intestinal fluid above pH 7.0, which method enhances the absorption of the active macromolecular principle due to the additive improving the solubility of the bile salt.

27. (previously presented) A pharmaceutical composition according to claim 31, wherein the enteric coating becomes permeable at a pH from 5.5 to 7.

28. (previously presented) A pharmaceutical composition according to claim 27, wherein the enteric coating becomes permeable at a pH from 5.5 to 6.5.

29. (previously presented) A method according to claim 32, wherein the enteric coating becomes permeable at a pH from 5.5 to 7.

30. (previously presented) A method according to claim 29, wherein the enteric coating becomes permeable at a pH from 5.5 to 6.5.

31. (previously presented) A composition according to claim 1, wherein the composition is coated with an enteric coating which becomes permeable at a pH from 3 to 7.

32. (previously presented) A method according to claim 26, wherein the composition is coated with an enteric coating which becomes permeable at a pH from 3 to 7

33. (previously presented) A composition according to claim 1, wherein the composition, when introduced into the intestine, enhances absorption of the active macromolecular principle due to the additive improving solubility of the bile salt.

34.-35. (canceled).

36. (previously presented) A composition according to claim 1, which is water soluble.

37. (previously presented) A method according to claim 26, wherein the composition is water soluble.

38. (previously presented) A composition according to claim 1, which is an oral pharmaceutical composition, and wherein, when the composition is introduced into the intestine, the additive (c) enhances the solubility of the non-conjugated bile salt.

39.-40. (canceled).

41. (previously presented) A composition according to claim 1, wherein the additive is capable of allowing the non-conjugated bile acid or salt to remain in solution when added to intestinal fluids at pH levels between 5 and 6.5.

42. (currently amended) A ~~composition~~method according to claim 26, wherein the additive is capable of allowing the non-conjugated bile acid or salt to remain in solution when added to intestinal fluids at pH levels between 5 and 6.5.